REMARKS

This Amendment is being filed with a Request for Continued Examination (RCE). Claims 16, 17, 24, 25, 27, 44, 46, 48, 50, 70, 71, 73-7, and 81-88 are pending. Of these, applicants have amended claims 24, 27, 44, 74, 76, and 84. Claims 1-15, 18-23, 26, 28-43, 45, 47, 49, 51-69, 72, 80, and 89-130 were cancelled in previous amendments or have been cancelled in the present amendment. These amendments add no new matter. In particular, the language added to claim 44 is supported in the specification as published (US 2006/0134599), e.g., at paragraph 0110, which describes the presently claimed devices as "a continuous flow cell sorter, e.g., that filters larger WBCs [white blood cells] and fetal RBCs [red blood cells] from blood," e.g., from adult, enucleated red blood cells. Other claim amendments correct dependencies and add full spelling for the acronym "FISH." These amendments also add no new matter.

35 U.S.C. § 102

Claims 16, 17, 25, 44-46, 48-50, 70-89, and 117-130 have been rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by newly cited Chou et al. (U.S. Patent No. 7,312,085 (hereinafter "Chou"). Applicants traverse this rejection for the following reasons.

According to the Office at page 3, Chou et al. describes "a method of producing a cell population enriched in a first type of cell larger than an adult, enucleated read blood cell, comprising flowing blood sample, through a channel in a microfluidic device comprising interchangeable steps of flowing the sample past obstacles in the channel, the obstacles fixed in position to obtained a first sample and then flowing the first sample past the obstacles for preferential binding of the first type of cell in the first sample to produce an enriched population of the first type of cells. Applicants first disagree with the Office's characterization that the various steps are "interchangeable," because the Office cites to no text in Chou to support that assertion, and in fact, the examples in Chou all provide a very specific order of steps constrained by the nature of the devices.

The Office next alleges that the claims are "identical to the cited disclosure and are considered to be anticipated by the teachings therein" (Office Action, page 3). Applicants

respectfully disagree and submit that Chou does not describe the method steps recited in currently amended independent claim 44, which recites:

> A method of producing a cell population enriched in a first type of cell larger than an adult, enucleated red blood cell, said method comprising:
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> continuously flowing a blood sample of a specific volume through a channel in a microfluidic device comprising;
>
> (i) continuously flowing the blood sample past a series of obstacles in the channel, the obstacles fixed in position separated by gaps arranged so that flow of the blood sample past the obstacles directs adult, enucleated red blood cells and cells smaller than adult, enucleated red blood cells in a first direction and directs cells larger than adult, enucleated red blood cells in a second direction to produce a first sample enriched in cells larger than adult, enucleated red blood cells; and without stopping the flow of the sample,
>
> (ii) continuously flowing the first sample past obstacles that each comprise one or more binding moieties that preferentially bind to the first type of cell in the first sample, thereby producing a population enriched in the first cell type.

While Chou describes various methods and techniques, and includes multiple examples, applicants submit that Chou fails to describe or suggest the presently claimed combination of steps. Chou does describe protrusions in the form of posts, and different microfluidic designs that can be used to manipulate cells, such as white blood cells and whole blood, but Chou's designs, as illustrated in Chou's figures, and described in detail in Examples 1 to 26, are all complex, relying on very specific flow paths defined and constrained by the devices. Of these many examples, the Office cites Example 26, at columns 103-108, illustrated in Figs. 84-88, which is said to be useful for sorting and analyzing blood samples. However, this example lacks any description of obstacles in the form of posts or otherwise and certainly does not describe any obstacles that include binding moieties. To the contrary, Example 26 refers to a "retention mechanisms" 1656 and 1658, both of which comprise a retention site, e.g., 1710, which is a "box"-like structure within the device, into which specific cells are directed to be retained (see Fig. 87, which shows this most clearly).

Furthermore, the Chou device is controlled by a complex system of valves (V1 to V10 in FIG. 85), and is thus not a continuous flow device as presently claimed. To the contrary, the liquid sample entering the Chou device shown in FIG. 85, moves from location to location within this complex device by a system of ten different valves, which halt the flow of the sample

at each point along its way through the Chou system. In particular, Chou describes filtration mechanism and then notes, "[a]fter suitable filtration, the larger particles may be released from filtration mechanism 1656 and moved by positioning mechanism 1654 toward retention mechanism 1658 (at column 104, lines 24-27, emphasis added)." This release mechanism is more clearly described as "filter release mechanism 1688 (valve V10)" which seals off capture chamber 1706 (at column 105, lines 35-47). See also FIG. 86. Similarly, there is a release mechanism 1662, which comprises valve V7 (see FIGs. 85 and 87), that controls the flow of the sample out of retention mechanism 1658 (see column 104, lines 32-35).

Given the complex system of valves as described in Chou's Example 26, there is simply no description of a continuous flow system as presently claimed. The presently claimed methods avoid the need for such separate capture chambers and valves to stop the flow of the sample, and provide a continuous flow design which is clearly not anticipated by Chou.

The Office also suggests that Chou discloses protrusions that are "fixed in position" and that are "treated for preferential binding of the cells." Applicants respectfully submit that to support an anticipation rejection, the Office cannot simply pick and choose from diverse embodiments described within the voluminous Chou application. Applicants are aware of no examples within Chou that recite the specific method steps currently recited in applicants' independent claim 44. The retention mechanisms in Chou are clearly mechanical holding chambers, with no suggestion that such holding chambers are treated in any way to include binding moieties, or even obstacles for that matter.

Thus, applicants respectfully request the Examiner to reconsider and withdraw this rejection under Section 102(e).

35 U.S.C. § 103

Claims 24 and 27 have been rejected as being allegedly unpatentable over Chou in view of Bogart, U.S. Patent No. 5,716,776 ("Bogart"), and Horne et al., U.S. Patent No, 6,974,667 ("Horne"). Applicants traverse this rejection for the following reasons.

According to the Office, these two claims differ from Chou in their specific limitations, but that Bogart describes a lysis solution containing bicarbonate and acetazolamide and that Horne describes an anti-CD36 binding moiety at col. 227, in Table 9B.

Applicants have amended these claims to correct typographical errors and to ensure that these two claims depend from claim 44. Thus, these two claims are patentable for at least the same reasons that claim 44 is patentable, and applicants request the Examiner to withdraw this rejection under Section 103.

Double Patenting

Claims 44, 45, 46, 58, 121, and 122 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16, 17, 19, 20-22, and 24 of copending Application No. 11/726,230. Applicants request that the double patenting rejection be held in abeyance until the claims are otherwise in condition for allowance.

CONCLUSION

By responding in the foregoing remarks only to particular positions taken by the Examiner, applicants do not acquiesce with other positions that have not been explicitly addressed. In addition, applicants' selecting some particular arguments for the patentability of a claim should not be understood as implying that no other reasons for the patentability of that claim exist. Finally, applicants' decision to amend or cancel any claim should not be understood as implying that applicants agree with any positions taken by the Examiner with respect to that claim or other claims.

In view of the foregoing amendments and remarks, applicants respectfully submit that the application is in condition for allowance, and such action is respectfully requested at the Examiner's earliest convenience.

The fees in the amount of $245 for a two-month extension of the period for response are being paid concurrently herewith on the Electronic Filing System by way of Deposit Account authorization. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 26118-0002US1.

Respectfully submitted,

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